REMARKS

Upon grant of the petition for revival submitted herewith, the application is currently pending. Further, upon entry of the foregoing amendment, claims 33-36, 38-39, and 44-45, are under examination, with claims 1-32, 37, 40-43 and 47-51 withdrawn by the Examiner under 37 C.F.R. § 1.142(b), and claim 46 canceled without prejudice to, or disclaimer of, the subject matter contained therein.

Claims 33-36, 38-39, and 33-45 are amended to improve the clarity of the wording. Claim 33 is amended to clarify that the array comprises: (i) a substrate; (ii) a binding surface which covers some or all of the substrate surface; and (iii) a plurality of protein expression systems located at discrete positions on the binding surface, wherein each expression system expresses at least one protein. Claim 33 is also amended to clarify the interaction of a particular component of a sample with proteins expressed by the array is measured by adding to the array a sample comprising at least one component to be assayed for its ability to interact with a protein expressed by at least one of the plurality of protein expression systems; and detecting an interaction of the sample component with a protein expressed by a specific protein expression system, wherein the step of detection comprises measurement of either the expressed protein or the sample component.

The amendments of claims 35, 36, 38, 44, and 45 are directed to improving the syntax of the claims. Claim 46 is canceled, since as noted by the Examiner, it is a duplicate of claim 44. Accordingly, no new matter is added by the claim amendments.

The specification is amended to correct the sections objected to by the Examiner. Thus, SEQ ID NOs. for sequences on pages, 18, 41-42 are included as requested by the Examiner. A sequence listing, as required under 37 C.F.R. 1.821, is also submitted

herewith. Also, paragraphs including embedded hyperlink have been amended to delete the hyperlink. The additional amendments correct wording of the abstract and typographical errors in the specification. Accordingly, no new matter is added by the amendments to the specification.

The Rejection of Claims Under 35 U.S.C. § 112 is Traversed or Rendered Moot

The Examiner rejected claims 33-36, 39, and 44-46 as allegedly being indefinite under 35 U.S.C. § 112, second paragraph. Thus, the Examiner stated that:

> A. It is not clear whether the "component of sample" in the preamble is the same as the "binding surface" in the body of the claims (ii). Also, the "protein expression array" is recited at step (a) but step (b) recites "protein expression systems". "The component" is unclear as to the reference made thereto.
>
> B. Claim 35 is unclear as to the location or determination of the "known" locations.
>
> C. Claim 38 "characterization of DNA" is inconsistent with the base claim, which does not recite DNA, but protein.
>
> D. It is not clear as to the biological or chemical products formed by the interaction of the component of the sample. The base claim recites a binding effect. Furthermore, the base claim does not recite "at least one component" of the sample

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Claim 33 is amended to improve the clarity of the claim and to clarify that the array comprises: (i) a substrate; (ii) a binding surface which covers some or all of the substrate surface; and (iii) a plurality of protein expression systems bound to discrete positions of the binding surface. Claim 33 is also amended to clarify the interaction of a particular component of a sample with proteins expressed by the array is measured by adding to the array a sample comprising at least one component to be assayed for its ability to interact with a protein expressed by at least one of the plurality of protein expression

systems, and detecting an interaction of the sample component with a protein expressed by a specific protein expression system, where the step of detection comprises measurement of either the expressed protein or the sample component. Thus, detection may comprise measurement of the sample component retained at the expression system, or binding of the sample component to the protein expressed by the expression system, or an increase in enzyme activity by an expressed protein (see the specification, e.g., at page 9, line 19 to page 10, line 5).

Claim 35 is amended to clarify that the proteins expressed by a first array may be transferred to "predetermined" locations on a second array such that the locations of proteins on the second array may be correlated with the location of an expression system on the first array, e.g., as described in the specification at page 15, line 8 to page 16, page 6. Claim 38 is amended to clarify that DNA may be isolated from an expression system from which an interaction between the sample component and a protein expressed by the expression system is found.

The Examiner did not refer to a specific claim in stating that "it is not clear as to the biological or chemical products formed by the interaction of the component of the sample" with the array. Claim 44, however, is amended to further clarify that the interaction of the at least one component of the sample with the expression array may be measured by ion mobility and time of flight mass spectroscopy detection of a biological or chemical product that is formed as the result of the interaction. As described in the specification (page 31, line 12 to page 33, line 15), an expressed protein that has bound a sample component and thus, has a larger molecular weight than the protein prior to binding the sample component, may be detected using ion mobility and time of flight mass spectroscopy.

The Rejection of Claims Under 35 U.S.C. § 102 is Traversed or Rendered Moot

The Examiner rejected claims 33-36 and 38-39 as allegedly anticipated bye Weiner et al. (WO 99/49294). Thus, the Examiner stated that:

> Weiner et al discloses at page 6, lines 13-25 a method in of screening a plurality of proteins that interact with a component of a sample comprising, generating a cDNA library created in E. coli, and comprising cDNA fused to the DNA sequence encoding the activation domain of the transcriptional activator, GAL4 protein, is plated onto agar plates. The E. coli colonies on each plate are pooled, plasmid DNAs are isolated, and the DNAs are used to transform yeast. The transformed yeast is plated onto solid medium and the colonies on each plate are pooled and aliquoted to separate wells of a 96-well microtiter plate to create an arrayed set of 10 "master library" plates. The master library set is re-aliquoted to create a "mating set" and a bait-containing yeast are then added separately to each well. The "bait" comprises a chimeric gene that expresses a hybrid protein containing the DNA-binding domain of GAL4 fused to a known protein. The host yeast strain contains the GAL1-lac-Z gene, which is able to bind the GAL4 DNA-binding domain. The GAL1-lacZ gene contains the E. coli lacZ gene encoding beta-galactosidase. The activity of beta-galactosidase is a measure of GAL4 function. Growth of yeast on galactose requires the transcription of genes regulated by GAL4 and is also a measure of GAL4 function.

Office Action at pages 5-6.

The assay described in Weiner et al., is an indirect assay that requires measurement of DNA expression of a third gene (beta-galactosidase; hereinafter "GAL") based on the interaction of two chimeric protein constructs, the first construct comprising the GAL DNA binding domain, and second construct comprising the GAL transcriptional activator, respectively, isolating the appropriate clone, and the analyzing the DNA. In contrast, Applicant's assay measures the interaction between a sample component and the expressed protein directly, by measurement of either the expressed protein or the sample component, and not by the indirect measurement of transcription of a third gene.

For at least these reasons, Applicants respectfully traverse the rejection under 35 U.S.C. § 102, and request that the rejection be withdrawn.

The Rejection of Claims Under 35 U.S.C. § 103 is Traversed or Rendered Moot

The Examiner rejected claims 33-36, 38-39, and 44-46 under 35 USC 103(a) as allegedly unpatentable over Weiner in view of Wagner et al. (US 6,329,209). Thus, the Examiner stated that:

> Weiner does not disclose measuring the interaction between the protein and the component in the sample by spectroscopy. However, Wagner discloses at col. 1, lines 56-60 the current technologies for the analysis of proteomes are based on a variety of protein separation techniques followed by identification of the separated proteins. The most popular method is based on 2D-gel electrophoresis followed by "in-gel" proteolytic digestion and mass spectroscopy. Said spectroscopy detection is further taught by Wagner at col. 34, line 7.

Office Action at page 6-7.

Applicant respectfully submits that there is nothing in Wagner which teaches or suggests the use of multidimensional spectroscopy (MDS) as a method to characterize products produced at particular addresses of the array. Wagner does describe some spectroscopy techniques that may be used to analyze protein arrays. Still, none of the techniques described in Wagner comprise two coupled detection systems (e.g., ion mobility and time-of-fight mass spectroscopy) that has the rapid time scale (milliseconds per sample) and the level of sensitivity of Applicants' invention. Also, time-of-flight spectroscopy systems provide the ability to directly couple high throughput detection to a biochip array. As described in the specification (e.g., page 33, lines 8-15), the multi-dimensional spectroscopic (MDS) technique of claim 44 allows for detection of

differences of as little as one unit mass or one unit ionic charge in a millisecond time frame. The application of MDS to array may allow for the quantification of on-going biochemical events, such as an enzyme reaction, or the nested separation of reaction components (see e.g., the specification at page 33 describing use of MDS in conjunction with ion mobility columns).

To establish a prima facie case of obviousness three criteria must be met: (i) a suggestion or motivation to modify or combine references; (ii) a reasonable expectation of success; and (iii) all the limitations in the claim(s) must be taught or suggested by the reference, or combination of references. MPEP 706.02(j). Applicants respectfully assert that neither of the references cited by the Examiner alone, or in combination, teach all of the limitations of Applicants' claimed invention. Nowhere in Wagner is the application of MDS to the processing of biological arrays taught or suggested. Nor is there any suggestion, upon reading these two references, to combine the references in a way that teaches Applicants' invention. Thus, Applicants respectfully assert that the cited references do not render Applicants' claimed invention unpatentable under 35 U.S.C. §103(a). For at least these reasons, Applicants respectfully traverse the rejection under 35 U.S.C. § 103, and request that the rejection be withdrawn.

CONCLUSION

In view of the foregoing amendment and remarks, each of the claims remaining in the application are in condition for immediate allowance. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the outstanding rejections.

The Examiner is respectfully invited to telephone the undersigned at (336) 747-7541 to discuss any questions relating to the application.

Respectfully submitted,

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